

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

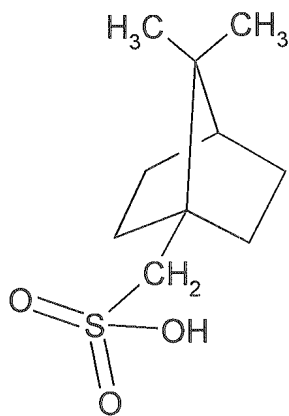
Appln. Of:	GEORGE KRSEK	)
Serial No.:	10/772,675	)
Filed:	February 4, 2004	)
For:	METHOD TO SEPARATE STEREOISOMERS	)
Group:	1723	)
Examiner:	DRODGE, JOSEPH	)
	DOCKET:	)
	KONEC 04.01	)

Commissioner of Patents & Trademarks  
Washington, D.C. 20231

**DECLARATION UNDER 37 CFR 1.132**

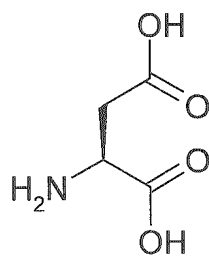
I, GEORGE R. KRSEK, Ph.D., hereby declare:

1. I am an Applicant in the above-referenced Application.
2. I prepared and/or purchased a variety of optically active acids, and attempted to use each of those optically active acids to resolve dl-methylphenidate.
3. Between July 9, 2001 and July 23, 2001, I unsuccessfully attempted to resolve dl-threo-methylphenidate using d-10-camphor sulfonic acid, compound I,



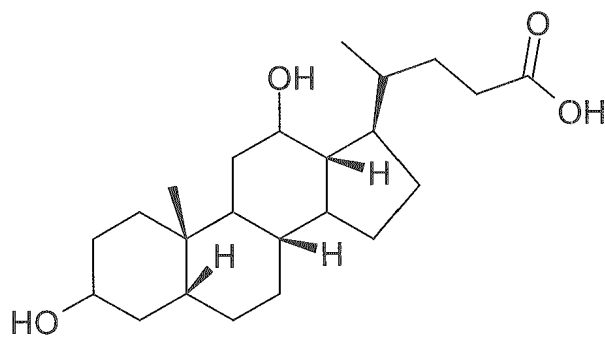
I

L-aspartic acid, compound II,



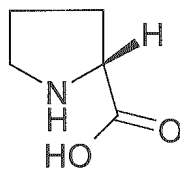
II

Deoxycholic acid, compound III



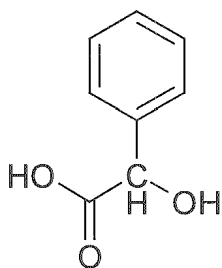
III

D-pyrrolidine carboxylic acid, compound IV,



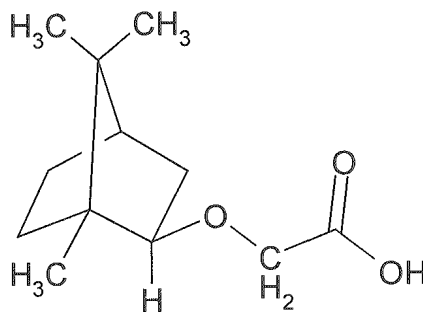
IV

and (+) Mandelic acid, compound V



V

4. On September 10, 2001, I attempted without success to resolve dl-threo-methylphenidate using (-) borneolxyacetic acid, compound VI



VI

5. Attachment "A" hereto recites data relating to the synthetic yield reported by Leffler and Calkins ("Leffler") for the preparation of *l*-menthoxyacetic acid from *l*-menthol, and data reported in the Application on Page 9 / Line 16 through Page 10 / Line 20 for my preparation of *l*-fenchyloxyacetic acid from *l*-fenchyl alcohol.

6. Attachment "B" hereto comprises true and accurate copies of Page 1188 and Page 1513 of the 2005-2006 Aldrich Catalog ("Aldrich").

7. Aldrich at Page 1188 recites a price for optically *l*-fenchyl alcohol of \$62.90 for 500 grams. See, Attachment "B" at Page 1188 - Product No. 196444-500G.

8. Aldrich at Page 1513 recites a price for *l*-menthol of \$94.50 for 500 grams. See, Attachment "B" at Page 1513 - Product No. M2780-500G-A.

9. Leffler reports a yield of 78-84% for the synthesis of *l*-menthoxyacetic acid from *l*-menthol. See, Leffler at Page 2.

10. I prepared 90 grams, or 0.48 moles, of *l*-fenchyloxyacetic acid using 200 grams, or 1.30 moles, of *l*-fenchyl alcohol for a yield of 36.90%. See, Application at Page 9 / Line 16 through Page 10 / Line 20.

11. Using the yield reported by Leffler and starting with 500 grams of *l*-menthol would give 475 grams of *l*-menthoxyacetic acid.

12. The price of *l*-menthoxyacetic acid produced, based on the cost of the starting *l*-menthol, would be \$0.20 per gram.

13. Using the method of Example 4 of the Application and starting with 500 grams of *l*-fenchyl alcohol would give 225 grams of *l*-fenchyloxyacetic acid.

14. The price of *l*-fenchyloxyacetic acid produced, based on the cost of the starting *l*-fenchyl alcohol, would be \$0.28 per gram.

15. The undersigned declares further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

  
GEORGE R. KRSEK, Ph.D.

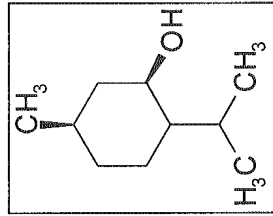
Date: 1 Nov 06

**CERTIFICATE OF ELECTRONIC FILING**

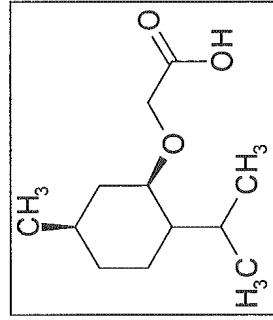
I hereby certify that on this 2nd day of November, 2006, the Declaration Under 37 CFR 1.132 is being filed via the Web Enabled Patent Filing System (EFT-WEB).

By: \_\_\_\_\_

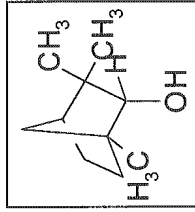
# ATTACHMENT “A”



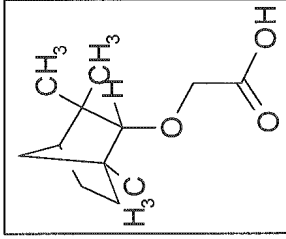
MENTHYL ALCOHOL  
MOL. WT. = 156 g/mole



MENTHOXYACETIC ACID  
MOL. WT. = 190 g/mole



FENCHYL ALCOHOL  
MOL. WT. = 154 g/mole



FENCHOXYACETIC ACID  
MOL. WT = 188 g/mole

STARTING ALCOHOL	PRICE FOR 500 G STARTING ALCOHOL	YIELD FOR OPTICALLY ACTIVE OXYACETIC ACID FROM STARTING ALCOHOL	YIELD IN GRAMS OF OPTICALLY ACTIVE OXYACETIC ACID STARTING WITH 500 G. ALCOHOL	PRICE PER GRAM BASED ON STARTING ALCOHOL
MENTHOL	\$94.50	78%	475 grams	\$0.20
FENCHYL ALCOHOL	\$62.90	36.80%	225 grams	\$0.28

# ATTACHMENT “B”



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# Aldrich

Advancing Science

2005-2006  
US

# Aldrich

■ Fatbrownrr ■

US \$

US \$

**Fat Brown RR**

[6416-57-5] CI 11285 C<sub>16</sub>H<sub>14</sub>N<sub>4</sub> FW 262.31  
**Dye content 95%**  
 mp . . . . . 147 to 158 °C  
 λ<sub>max</sub> . . . . . 451 nm  
 R: 36/37/38 S: 26-36 RTECS# ST2900000; TSCA

236039-25G glass btl 25 g 31.00

**Fatty acid methyl esters/C<sub>6</sub>-C<sub>24</sub>, straight-chain, kit containing 19 standards**

25,222-0 Methyl arachidate 1g  
 85,527-8 Methyl behenate 500mg  
 25,994-2 Methyl caproate 2.5mL  
 26,067-3 Methyl caprylate 2.5g  
 29,903-0 Methyl decanoate 2.5g  
 14,900-4 Methyl enanthate 2.5mL  
 28,607-9 Methyl heptadecanoate 250mg  
 29,904-9 Methyl heneicosanoate 100mg  
 23,459-1 Methyl laurate 2.5g  
 14,898-9 Methyl myristate 2.5g  
 28,683-4 Methyl nonadecanoate 500mg  
 24,589-5 Methyl nonanoate 2.5g  
 26,065-7 Methyl palmitate 1g  
 23,545-8 Methyl pentadecanoate 2.5g  
 M8,070-9 Methyl stearate 1g  
 29,905-7 Methyl tetracosanoate 100mg  
 28,734-2 Methyl tricosanoate 100mg  
 M8,540-9 Methyl tridecanoate 2.5g  
 29,941-3 Methyl undecanoate 2.5g

299022-1KT 1 kit 400.80

**Fatty acids/C<sub>6</sub>-C<sub>24</sub>, straight-chain, kit containing 19 standards**

E23-1 Arachidic acid  
 21,694-1 Behenic acid  
 15,376-1 Decanoic acid  
 15,378-8 Dodecanoic acid  
 21,966-5 Heneicosanoic acid  
 H100-0 Heptadecanoic acid  
 25,873-3 Heptanoic acid  
 15,374-5 Hexanoic acid  
 15,379-6 Myristic acid  
 N5252 Nonadecanoic acid  
 N2,990-2 Nonanoic acid  
 15,375-3 Octanoic acid  
 25,872-5 Palmitic acid  
 P360-0 Pentadecanoic acid  
 26,838-0 Stearic acid  
 23,468-0 Tetracosanoic acid  
 21,859-6 Tricosanoic acid  
 T0502 Tridecanoic acid  
 17,147-6 Undecanoic acid  
 R: 34 S: 26-28-36/37/39-45

298514-1KT 1 kit 286.20

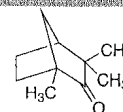
**Fenbuten, 96%**

[36330-85-5] C<sub>6</sub>H<sub>5</sub>C<sub>6</sub>H<sub>4</sub>CO(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H FW 254.28  
 Merck 13,3990  
 mp . . . . . 184 to 187 °C  
 R: 25 S: 28-45 RTECS# DV1761000

538515-1G glass btl 1 g 21.90  
 538515-5G glass btl 5 g 72.90

**(1R)-(-)-Fenchone, ≥98%**

(-)-Fenchone; (-)-1,3,3-Trimethyl-2-norbornanone  
 [7787-20-4] C<sub>10</sub>H<sub>16</sub>O FW 152.23  
 [α]<sub>D</sub><sup>24</sup> -50.5°, neat  
 Beil. 7,IV,212; Fieser 8,228  
 bp. . . . . 192-194 °C  
 density . . . . . 0.948 g/mL 25 °C  
 mp . . . . . 5 to 6 °C  
 n<sub>D</sub><sup>20</sup> . . . . . 1.461  
 R: 10 S: 23-24/25; TSCA Fp: 52°C (126°F)



196436-50G glass btl 50 g 23.30  
 196436-250G glass btl 250 g 73.30

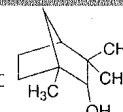
**(+)-Fenchone, ≥98.0% (GC, sum of enantiomers)**

(1S)-1,3,3-Trimethylbicyclo[2.2.1]heptan-2-one; (+)-1,3,3-Trimethyl-2-norbornanone  
 [4695-62-9] C<sub>10</sub>H<sub>16</sub>O FW 152.23  
**purum**  
 [α]<sub>D</sub><sup>20</sup> +60±3°, neat  
 Merck 13,3995; Beil. 7,IV,212  
 bp. . . . . 63-65 °C/13 mm Hg mp . . . . . 5 to 7 °C  
 density . . . . . 0.945 g/mL 20 °C  
 mp . . . . . 5 to 7 °C n<sub>D</sub><sup>20</sup> . . . . . 1.463  
 S: 23-24/25 RTECS# RB7875200 Fp: 66°C (151°F)

46210-100ML-F 100 mL 115.10

**(1R)-endo-(+)-Fenchyl alcohol, 96%**

(+)-Fenchol  
 [2217-02-9] C<sub>10</sub>H<sub>18</sub>O FW 154.25  
 Beil. 6,IV,278  
 mp . . . . . 39 to 45 °C  
 S: 22-24/25 Fp: 74°C (165°F)



196444-5G glass btl 5 g 18.90  
 196444-100G glass btl 100 g 20.30  
 196444-500G glass btl 500 g 62.90

☑ **Fenoxaprop ethyl**, see Ethyl (2S)-(+)-2-[4-(6-chlorobenzoxazol-2-yl)oxy]phenylpropanoate Page 1128  
**Ferene**®, see 3-(2-Pyridyl)-5,6-bis(5-sulfo-2-furyl)-1,2,4-triazine disodium salt Page 2054  
**Ferric ammonium citrate**, see Ammonium iron(III) citrate Page 224

**Ferric citrate**

[3522-50-7] FeC<sub>6</sub>H<sub>5</sub>O<sub>7</sub> FW 244.94  
 Fe 16.5-18.5%  
 light sensitive

F6129-250G 250 g 30.60  
 F6129-1KG 1 kg 100.30

**Ferric hydroxide oxide**

[20344-49-4] Fe(OH)<sub>3</sub> FW 88.85  
 Merck 13,4055  
 TSCA

**crystalline powder, 50-80 mesh**

546267-50G poly btl 50 g 45.70  
 546267-250G poly btl 250 g 170.00

**catalyst grade, 30-50 mesh**

371254-50G poly btl 50 g 47.00  
 371254-250G poly btl 250 g 178.50

**Ferrocene**

[102-54-5]  
 Merck 13,40  
 bp. . . . .  
 mp . . . . .  
 λ<sub>max</sub> . . . . . R: 11

408-5G  
 408-100G  
 408-500G

**Ferrocene**

[1287-16-7]  
 Beil. 16,IV,1  
 mp . . . . .

335045-50G

**Ferrocene**

[1316-91-2]  
 Beil. 16,IV,1  
 mp . . . . . R: 2021

335053-1G

335053-5G

**Ferrocene**

[12152-94-2]  
 Contains var  
 mp . . . . . R: 36/37

455547-5G

455547-25G

**Ferrocene**

[12093-10-6]  
 Beil. 16,IV,1  
 mp . . . . . S: 22-24/25

122459-1G

122459-5G

122459-25G

**Ferrocene**

[1271-42-7]  
 Beil. 16,IV,1  
 mp . . . . .  
 106887-1G  
 106887-10G

**1,1'-Ferrocene**

C<sub>22</sub>H<sub>22</sub>B<sub>2</sub>O<sub>4</sub>F  
 mp . . . . . S: 22-24/25

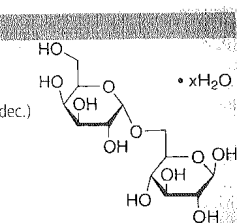
643750-1G

643750-10G

**1,1'-Ferrocene**

[1271-48-3]  
 mp . . . . .  
 496391-500G

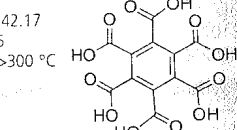
US \$



5 g	34.00
10 g	59.10
25 g	117.50
100 g	295.50

FW 452.80

92 to 94 °C	
glass btl 100 mg	37.10
glass btl 1 g	264.50



glass btl 1 g 39.90

to 300°C, kit containing 24

34-136°C  
-286°C  
1°C  
°C  
id 198-200°C  
dinitrophenylhydrazine 159-

methoxyphenol 70-73°C  
40-241°C  
ene 59-61°C  
id 209-210°C

21°C  
e 128-130°C  
acid 270-272°C  
acid 248-252°C  
C  
9-262°C  
86°C  
70-172°C  
glutamic acid 180-181°C  
113°C  
benzoic acid 219-220°C  
150-152°C

1 kit 290.40

methoxymethyl chloride Page 1544  
ce (+)-Pentylaldehyde Page 1824  
R(-)-α-Phellandrene Page 1827

US \$

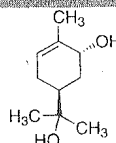
**trans-p-Menth-6-ene-2,8-diol, 99%**[42370-41-2] C<sub>10</sub>H<sub>18</sub>O<sub>2</sub> FW 170.25

Beil. 6,752

bp. . . . . 270-271 °C

mp. . . . . 130 to 132 °C

RTECS# F12000000



247774-10G	glass btl 10 g	29.70
247774-50G	glass btl 50 g	91.60

**(+)-p-Menth-1-en-9-ol, mixture of isomers, 97%**[18479-68-0] C<sub>10</sub>H<sub>18</sub>O FW 154.25

(R,R)-isomer ~67%, (R,S)-isomer ~33%

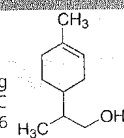
[α]<sub>D</sub><sup>20</sup> +99°, c = 4.2 in C<sub>6</sub>H<sub>5</sub>CH<sub>3</sub>

bp. . . . . 115-116 °C/10 mm Hg

density . . . . . 0.941 g/mL 25 °C

n<sub>D</sub><sup>20</sup> . . . . . 1.486

TSCA Fp: 103°C (218°F)



183741-1G	glass btl 1 g	26.10
183741-10G	glass btl 10 g	155.50

**(-)-Menthofuran, >90% (GC)**

(R)-3,6-Dimethyl-4,5,6,7-tetrahydrobenzofuran

[17957-94-7] C<sub>10</sub>H<sub>14</sub>O FW 150.22

technical

[α]<sub>D</sub> +97±5°, neat

Beil. 17,V,1,518

bp. . . . . 204-206 °C density . . . . . 0.97 g/mL 20 °C

57594-25ML-F 25 mL 96.70

**Menthol, 99%**[89-78-1] C<sub>10</sub>H<sub>20</sub>O FW 156.27

Merck 13,5861; Beil. 6,IV,151; Fieser 13,172

bp. . . . . 216 °C mp. . . . . 34 to 36 °C

density . . . . . 0.89 g/mL 25 °C vp. . . . . 0.8 mm Hg (20 °C)

R: 37/38-41 S: 26-36 RTECS# OT0350000 Fp: 93°C (200°F)

M2772-5G-A	glass btl 5 g	21.00
M2772-100G-A	glass btl 100 g	23.50
M2772-500G-A	glass btl 500 g	78.20

**Menthol solution****NMR reference standard, 30 wt. % in chloroform-d (99.8 atom % D)**

APT &amp; Dept demonstration

R: 22-38-41-48/20/22 S: 36/37/39 Hygroscopic

551376-1EA	5mm x 8in. 1 ea	116.00
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**LC-NMR reference standard, 50% in chloroform-d (99.9 atom % D), chromium(III) acetylacetonate 0.5%**

R: 22-38-40-41-48/20/22 S: 36/37/39 Hygroscopic, Light sensitive

613290-1EA	5mm x 8in. 1 ea	318.00
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**(1R,2S,5R)-(-)-Menthol**[2216-51-5] C<sub>10</sub>H<sub>20</sub>O FW 156.27

Beil. 6,IV,150; Fieser 12,294; 13,172; 16,203

bp. . . . . 212 °C

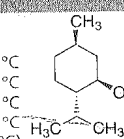
density . . . . . 0.89 g/mL 25 °C

mp. . . . . 41-44 °C

vp. . . . . 42 to 45 °C

0.8 mm Hg (20 °C)

R: 37/38-41 S: 26-39 RTECS# OT0700000 Fp: 101°C (214°F)



99%

[α]<sub>D</sub><sup>20</sup> -50°, c = 10 in C<sub>2</sub>H<sub>5</sub>OH

ee: 99% (GLC)

**■ Menthylace ■**

M2780-25G-A	poly btl 25 g	14.30
M2780-100G-A	poly btl 100 g	29.20
M2780-500G-A	poly btl 500 g	94.50

**>99%, sublimed**[α]<sub>D</sub><sup>20</sup> -50°, c = 10 in CH<sub>3</sub>CH<sub>2</sub>OH

TSCA

588733-1G	glass btl 1 g	34.50
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**(1S,2R,5S)-(+)-Menthol, 99%**

(+) -Menthol

[15356-60-2] C<sub>10</sub>H<sub>20</sub>O FW 156.27[α]<sub>D</sub><sup>23</sup> +48°, c = 10 in C<sub>2</sub>H<sub>5</sub>OH

ee: 96% (GLC)

Beil. 6,IV,151; Fieser 12,294; 13,172

bp. . . . . 103-104 °C/9 mm Hg vp. . . . . 0.8 mm Hg (20 °C)

mp. . . . . 43 to 44 °C

R: 37/38-41 S: 26-36 RTECS# OT0700000; TSCA

Fp: 101°C (214°F)

224464-10G	glass btl 10 g	33.30
224464-50G	glass btl 50 g	110.50

**(-)-Menthone, 90%**[14073-97-3] C<sub>10</sub>H<sub>18</sub>O FW 154.25[α]<sub>D</sub><sup>20</sup> -20°, neat

Merck 13,5862; Beil. 7,IV,87; Fieser 14,201;

16,204

bp. . . . . 207-210 °C

density . . . . . 0.893 g/mL 25 °C

vp. . . . . 0.5 mm Hg (20 °C)

n<sub>D</sub><sup>20</sup> . . . . . 1.45

isomenthone . . . . . 5%

S: 23-24/25; TSCA Fp: 72°C (162°F)

218235-25G	glass btl 25 g	23.60
218235-100G	glass btl 100 g	54.00

**(-)-Menthoxycarbonyl chloride, 97%**[15356-62-4] C<sub>12</sub>H<sub>21</sub>ClO<sub>2</sub>

FW 232.75

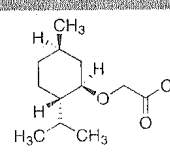
[α]<sub>D</sub><sup>25</sup> -10°, neat

density . . . . . 1.033 g/mL 25 °C

n<sub>D</sub><sup>20</sup> . . . . . 1.469

R: 34 S: 26-27-36/37/39-45

Fp: 113°C (235°F)



453714-1G	glass btl 1 g	23.90
453714-5G	glass btl 5 g	79.80

**Menthyl acetate, 97%**[89-48-5] C<sub>12</sub>H<sub>22</sub>O<sub>2</sub> FW 198.30

Merck 13,5863; Beil. 6,II,50

bp. . . . . 228-229 °C n<sub>D</sub><sup>20</sup> . . . . . 1.447

density . . . . . 0.922 g/mL 25 °C

TSCA Fp: 92°C (198°F)

422770-25ML	glass btl 25 mL	21.90
422770-100ML	glass btl 100 mL	60.70

**(1R)-(-)-Menthyl acetate, 98%**[2623-23-6] C<sub>12</sub>H<sub>22</sub>O<sub>2</sub> FW 198.30[α]<sub>D</sub><sup>20</sup> -81°, c = 8 in C<sub>6</sub>H<sub>6</sub>

ee: 98% (GLC)

Beil. 6,IV,153

bp. . . . . 229-230 °C n<sub>D</sub><sup>20</sup> . . . . . 1.447

density . . . . . 0.92 g/mL 25 °C

RTECS# AI5900000; TSCA Fp: 77°C (171°F)

441058-25ML	glass btl 25 mL	24.60
441058-100ML	glass btl 100 mL	65.60